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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/091,300	03/04/2002	Patricia Rockwell	11245/46211	1694

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KENYON & KENYON
ONE BROADWAY
NEW YORK, NY 10004

EXAMINER

BLANCHARD, DAVID J

ART UNIT	PAPER NUMBER
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1642

DATE MAILED: 09/03/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/091,300

Applicant(s)

ROCKWELL ET AL.

Examiner

David J Blanchard

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 22 June 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-67 is/are pending in the application.
- 4a) Of the above claim(s) 6, 10, 15, 18, 22, 27, 29-61 and 63-66 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-5, 7-9, 11-14, 16-17, 19-21, 23-26, 28, 62 and 67 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- ☐ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____.
- ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- ☐ Notice of Informal Patent Application (PTO-152)
- ☐ Other: _____.

DETAILED ACTION

1. Claims 1-67 are pending.

Claims 1, 11, 23, 25-26 and 62 have been amended.

Claims 6, 10, 15, 18, 22, 27, 29-61 and 63-66 have been withdrawn.

2. Claims 1-5, 7-9, 11-14, 16-17, 19-21, 23-26, 28, 62 and 67 are pending and under examination.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Objections/Rejections Withdrawn

4. The objections to the specification for not containing US patent numbers for USSNs 09/401,163, 08/967,113 and 07/813,593 are withdrawn in view of the amendments to the specification filed 6/22/2004.
5. The objection to claims 1 and 62 as being drawn to non-elected inventions is withdrawn in view of the amendments to the claims filed 6/22/2004.
6. The rejection of claims 1-5, 7-9, 11-14, 16-17, 19-21, 23-26, 28, 62 and 67 under 35 U.S.C. 103(a) as being unpatentable over Rockwell et al in view of Queen et al and Fan et al and Siemeister et al is withdrawn in view of Applicant's arguments.

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Response to Arguments

7. The rejection of claims 1-5, 7-9, 11-14, 16-17, 19-21, 23-26, 28, 62 and 67 under 35 U.S.C. 103(a) as being unpatentable over Rockwell et al in view of Petit et al as evidenced by Kawamoto et al is maintained.

The response filed 6/22/2004 has been carefully considered, but is deemed not to be persuasive for the reasons of record set forth in the previous Office Action and addressed herein. The response argues that although the Office alleges that it is prima facie obvious to combine two components that are taught by the prior art to be useful for the same purpose, anti-VEGFR antibodies and anti-EGFR antibodies are not recognized in the art as equivalents. Applicant argues that because the two antibodies bind to and inhibit two different receptors they cannot be considered functionally or structurally equivalent. Applicant admits that Petit et al teaches that an anti-EGFR antibody functions to inhibit expression of the VEGFR ligand, VEGF, and again argues that this does not lead to the conclusion that the art recognizes anti-EGFR antibodies and anti-VEGFR antibodies as equivalents. Applicant argues that for the two antibodies to be considered equivalents, there must be some teaching or suggestion in the art that an anti-EGFR antibody will bind with VEGFR and prevent its ligands from binding the receptor and the anti-VEGFR antibody will bind EGFR and prevent its ligands from binding the receptor. In response to applicant's arguments that there is no suggestion to combine the references (i.e., that the two antibodies are not recognized as functional equivalents), the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the art to produce the claimed invention where

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there is some teaching, suggestion or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art.

See In re Fine 5 USPQ2d 1596 (Fed Cir 1988) and In re Jones 21 USPQ2d 1941 (Fed Cir 1992).

The examiner recognizes that the anti-VEGFR antibodies and anti-EGFR antibodies are not structurally and functionally equivalent in that they recognize different receptors, however, both anti-VEGFR and anti-EGFR antibodies are functional equivalents with respect to inhibiting the interaction between the VEGF receptor (VEGFR) and its ligand, VEGF, and ultimately inhibit tumor growth. Applicant is reminded that the test for combining references is what the combination of disclosures taken as a whole would suggest to one of ordinary skill in the art In re McLaughlin, 170 USPQ 209 (CCPA 1971). References are evaluated by what they suggest to one versed in the art, rather than by their specific disclosures. In re Bozek, 163 USPQ 545 (CCPA 1969). In the instant case Rockwell et al teaches that neutralizing anti-VEGFR antibodies inhibit tumor growth by inhibiting the interaction between the VEGFR and VEGF and "the combined treatment of one or more of the antibodies of the invention with an anti-neoplastic or chemotherapeutic drug, such as, for example, doxorubicin, cisplatin or taxol provides an even more efficient treatment for inhibiting the growth of tumor cells than the use of the antibody itself (column 7, lines 17-27) and Petit et al teach that VEGF is a tumor angiogenesis factor and EGFR as an inducer of VEGF and a chimeric version of the anti-EGFR 225 antibody (C225) reduces VEGF expression. Clearly, it would have been obvious to one of ordinary skill in the art at the time the

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invention was made that the anti-EGFR antibody, C225 would decrease the expression of the tumor angiogenesis factor VEGF as taught by Petit et al, thereby inhibiting the interaction between VEGFR and VEGF and hence, by extension tumor angiogenesis (tumor growth). Therefore, the combined teachings of Rockwell et al and Petit et al would have led one of ordinary skill in the art at the time the invention was made to combine the anti-VEGFR and anti-EGFR antibodies to synergistically inhibit the VEGFR-VEGF interaction and hence, tumor growth with an expectation of success.

Again, it is prima facie obvious to combine two compositions (anti-VEGFR antibody and anti-EGFR antibody) each of which is taught by the prior art to be useful for the same purpose (i.e., inhibiting the interaction between VEGFR and VEGF and ultimately inhibiting tumor growth) in order to form third composition that is to be used for very same purpose; idea of combining them flows logically from their having been individually taught in prior art. In re Kerkhoven, 205 USPQ 1069, CCPA 1980. See MPEP 2144.06.

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., that an anti-EGFR antibody will bind with VEGFR and prevent its ligands from binding the receptor and the anti-VEGFR antibody will bind EGFR and prevent its ligands from binding the receptor) are not recited in the rejected claims.

The response also argues that there is no teaching or suggestion in the references cited that the different treatment plans could be combined without losing their selectivity and activity against tumor cells, while their effect on normal cells is

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unknown. The response argues that the skilled artisan would not consider combining the anti-VEGFR and anti-EGFR antibodies in a kit based on the teachings or suggestions in the cited references. In response to the first argument, the examiner is unclear as to applicant's argument. It appears that applicant is arguing that combining the two antibodies in a treatment method would result in the two antibodies losing their selectivity and activity against tumor cells, while their effect on normal cells is unknown. In response to this argument the skilled artisan would have combined the two antibodies to inhibit the VEGFR-VEGF interaction and inhibit tumor growth as discussed above. Absent evidence to the contrary, the skilled artisan would have combined the two antibodies knowing that the anti-EGFR antibody would specifically bind the EGFR and the anti-VEGFR antibody would specifically bind the VEGFR. With respect to applicant's argument pertaining to kits, it is reiterated that there is no positive recitation of the kit ingredients/elements that distinguishes the claim over the references and it would have been obvious to one of ordinary skill in the art to place the recited antibodies in a kit for the advantages of convenience and economy.

From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

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8. The rejection of claims 1, 5, 7-8, 11-14, 17, 19-21, 23-26, 28, 62 and 67 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 2, 15, 17, 25-26 and 32 of copending Application no. 09/798,689 in view of Queen et al is maintained.

The response filed 6/22/2004 has been carefully considered, but is deemed not to be persuasive. The response states that Applicant will file a Terminal Disclaimer upon issuance of the 09/798,689 application, which was recently allowed. In response to this argument no Terminal Disclaimer has been filed and as such the rejection is maintained.

Conclusions

9. No claim is allowed.

10. Applicant's amendment necessitated the new grounds of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any


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extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Blanchard whose telephone number is (571) 272-0827. The examiner can normally be reached at Monday through Friday from 8:00 AM to 6:00 PM, with alternate Fridays off. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew, can be reached at (571) 272-0787. The official fax number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Respectfully,
David J. Blanchard
571-272-0827


LARRY R. HELMS, PH.D
PRIMARY EXAMINER